NEURO-HISTOLOGICAL FINDINGS IN OSTEOPETROSIS (ALBERS-SCHÖNBERG DISEASE)*

BY

F. VRABEC AND J. SEDLÁČKOVÁ

From the Eye Clinic of the Medical Faculty of Hygiene of the Charles University, Prague

OSTEOPETROSIS (Albers-Schönberg disease; marble bones) is a very rare condition with a strong familial tendency. The majority of cases so far published are to be found in the roentgenological or paediatric literature, some of them with more or less detailed ophthalmological findings. The most striking feature of the disease is the excessive calcification of the osteoid tissue with the absence of true ossification (Boyd, 1953). Spontaneous fractures are common. There is a narrowing of the medullary cavity leading to osteosclerotic anaemia, associated sometimes with extramedullary haematopoiesis. From the ophthalmological point of view this condition is interesting for the following reasons:

(1) There exists very often an atrophy of the optic nerve with or without excavation of the optic nervehead, sometimes associated (Pietruschka, 1958) with a degree of papilloedema;

(2) Diminished power of convergence results occasionally in a divergent squint, and a convergent squint may be rarely noted (McCune and Bradley, 1934).

Other eye symptoms include lagophthalmos (Pietruschka, 1953), slight exophthalmos, nystagmoid movements of the globes, and diminution or even abolition of the pupillary light reflex. In some cases a certain degree of hypertelorism was noted; Pietruschka found a moderate hypalgesia in the area innervated by the left trigeminal nerve, with preservation of the corneal reflex. When the determination of peripheral vision was possible, central relative scotoma or concentric peripheral contraction of visual fields was found. Pietruschka observed, in one of his four cases, a pronounced narrowing of the retinal arteries.

A report of the neuro-histological findings in the eye as well as in the extra-ocular muscles of such a case is still sufficiently rare to warrant publication. We were able to observe this patient with a malignant early infantile type of this rare condition owing to the kindness of Prof. Dr. J. Čížková, director of the Paediatric Clinic of our faculty.

Case Report

A girl born on August 22, 1962, is the third child of the family. The first child is now 6 years old without any signs of the disease, except for a slight degree of hypertelorism. The second child died at birth. The birth weight of this third child was 3·400 g. At one month(?) she had an attack of convulsions and these increased in frequency. She was therefore admitted to the Paediatric Clinic.

* Received for publication June 24, 1963.

Examination.—There was an enlargement of the liver together with a “blowing” type of respiration. During this examination the patient had convulsions with loss of consciousness. X ray of the chest showed characteristic bone changes, and the diagnosis of Albers-Schönberg disease was subsequently confirmed by x rays of the skull (Figs 1 and 2) and extremities.

FIG. 1.—Postero-anterior x ray, showing increased density of the bones of the base of the skull and the face.

FIG. 2.—Lateral x ray, showing encroachment of the bony changes on the sella turcica and thickened clinoid processes.

The blood showed a moderate leucocytosis with progressive aplastic anaemia.

A neurological examination showed generalized spasms without topical signs and oedema of the brain was suspected.

Ophthalmological Findings.—The anterior segments of both eyes were normal; both optic nerve-heads were white and sharply demarcated, with pronounced excavation.

Death.—At the age of 3 months the patient died from anaemia with extramedullary haematopoiesis and brain oedema.

Autopsy

We were able to examine both eyes. After formalin fixation one eye was cut in the sagittal plane and a 3-mm. thin slice of the whole eye was embedded in paraffin. Both remaining lateral parts together with the dissected anterior and posterior halves of the other eye were cut tangentially on a freezing microtome and the sections were impregnated by the method of Gros-Schultze; other sections were stained by the myelin method of Spielmeyer.

Findings.—In the paraffin sections the only abnormalities were signs of delayed regressive changes in the mesoderm of the anterior chamber angle and in the anterior layer of the iris. The anterior tendons of the ciliary muscle were mostly directly attached to the uveal portion of the trabecular meshwork, the latter being still of a definite foetal pattern.

The retina showed a remarkable loss of the elements of the ganglion cell layer. The other neurons—bipolar and visual cells—were much better preserved.

Both optic nerves were atrophied but for a small sector of partially preserved neurofibrils (Figs 3 and 4). The intervaginal spaces of both optic nerves were not enlarged. The connective tissue septa of the optic nerve was coarse, and in the fields between them a massive gliosis was present. The connective tissue surrounding the central vessels of the optic nerve seemed a little hypertrophied; the structure of the vessel walls showed no change. The connective tissue septa of the optic nerve were coarser, even in the sector with preserved neurofibrils, and the latter did not appear to be so numerous as in normal subjects. Some fine, non-myelinated nerve fibres apparently without degenerative changes were found in the tissue of the dural sheath and the connective septa.

FIGS 3 and 4.—Sections of optic nerve showing atrophy and small sector of partly preserved neurofibrils.

Spielmeyer's stain for myelin revealed no trace of myelin sheaths even in the sector of preserved neurofibrils. The other optic nerve was cut longitudinally but even here only a narrow sector of partially-preserved neurofibrils without myelin and with a massive gliosis was noted.

The posterior ciliary nerves were mostly quite well preserved (Fig. 5, opposite): their myelin sheaths were conspicuous, with no sign of degeneration. Some fine branches of the ciliary nerves showed varicose swellings (Fig. 6, opposite), but we were able to trace them only in the posterior half of the eye.

Most of the fibres forming the supraciliary plexus were preserved and in a still better condition were those of the corneal nerve trunks (Fig. 7, opposite), where we failed to find any degenerate fibres at all. It seems probable, therefore, that some of the so-called varicose nerve fibres were mostly fine autonomic nerve fibres supplying the choroidal vessels, or the intramural ganglion cells scattered through the whole choroid in large numbers. We should like to mention here the very small proportion of fine non-myelinated fibres in the supraciliary nerve plexus, the proportion of such fibres being much smaller than in a normal eye,

FIG. 5.—Posterior ciliary nerve.

FIG. 6.—Varicose swellings in five branches of ciliary nerves.

FIG. 7.—Fibres of corneal nerve trunks.

FIG. 8.—Nerve supply of extra-ocular muscle.

though the exact number to be expected at this age and in normal conditions is not known. Kolmer (1936) could find hardly any ganglion cells in the ciliary plexus of a newborn infant but such elements were very numerous in an adult eye.

The subepithelial or basal epithelial nerve plexus of the cornea was normal.

The nerve supply of many of the extra-ocular muscles was quite rich (Fig. 8), with the main nerve trunks and their first branches apparently in good condition. In following their course, however, we detected some regions with early degenerative changes of the nerve fibres revealing varicosities or even fragmentation of axons in the form of rows of argyrophilic grains. The motor plates stained only faintly and occasionally some of them seemed to be degenerate as well, only our knowledge of their development in such a baby is still unsatisfactory.

Considering the very late myelination of the optic nerve fibres (reaching the level of the lamina cribrosa at the time of birth), it seems to us very difficult to ascertain whether the

myelin sheaths of the optic nerve fibres in this case had been lost by degeneration or had simply not developed.

Comment

It is difficult to ascertain whether the myelin sheaths of the optic nerve fibres were lost by degeneration, or whether they simply did not develop at all, reaching the level of the lamina cribiformis just at the moment of birth. The high percentage of nerve fibres lost by atrophy as well as the poor preservation of the ganglion cells of the retina suggest that the degenerative process had begun well before birth. It would seem reasonable, therefore, to assume that the process of myelination was impaired before reaching the periphery. The sensory innervation of the ciliary muscle, cornea, and extra-ocular muscles was normal. The motor nerve supply of the extra-ocular muscles showed early signs of degeneration restricted to certain limited regions. We can assume, therefore, that the motor function of the extra-ocular muscles would deteriorate much earlier than the sensory innervation. The innervation pattern of the ciliary muscle did not suffer, and we have not noticed that an early loss of accommodative power was observed in the young patients so far reported.

The atrophy of the optic nerve fibres in our patient should be attributed either to the narrowing of the optic nerve canals from the condensation of the base of the skull, or to the pressure or traction exerted by the thickened anterior clinoid processes. The second alternative is supported by the form of the preserved sector of intact nerve fibres in both optic nerves as well, perhaps, as by the narrowing of the retinal arteries reported by Pietruschka in one of his cases. We have noted similar spastic changes in the retinal arteries in other cases of chiasmal lesions; we were able to follow a very distinct—symmetrical—narrowing of the retinal arteries in a case of cholesteatoma of the base of the skull.

Summary

A case of early infantile malignant osteopetrosis with histological as well as neuro-histological findings in both globes and in the extra-ocular muscles is described; the most pronounced changes were found in the optic nerves. In the ciliary nerves and in the motor nerves of the extra-ocular muscles, only localized signs of degeneration of the fine nerve fibres were noted. The innervation of the ciliary muscles as well as of the corneae was quite normal. All the findings agree with the clinical course of most cases hitherto described.

REFERENCES

- BOYD, W. (1953). "A Text-book of Pathology", 6th ed., p. 916. Kimpton, London.
 KOLMER, W. (1936). In "Handbuch der mikroskopische Anatomie des Menschen", bd 3, teil 2, "Auge", p. 86.
 MCCUNE, D. J., and BRADLEY, C. (1934). *Amer. J. Dis. Child.*, **48**, 949.
 PIETRUSCHKA, G. (1953). *Klin. Mbl. Augenheilk.*, **123**, 189.
 ——— (1958). *Ibid.*, **132**, 509.
 RISER, R. O. (1941). *Amer. J. Ophthal.*, **24**, 874.